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well-defined types of information flow between them during execution of the program. For example, a program that tracks credit card accounts usually has to know in what kind of memory device the accounts are kept and the location in memory of each account. In an unstructured program, this information must be available every time an account is accessed. In a modular, structured program, only one module needs to keep this information. Every other module that manipulates an account in any way only has to know that it can be reached through the module that has this information. Besides making the program easier to write, modularity means that usually changes in the program can be confined to the module involved.

This characteristic of Ada is directly reflected in the design of the micromainframe by way of its object-oriented architecture. Architecture is computer jargon for design—how information flows through the machine as seen by the programmer. As one attendee at the solid-state circuits conference told *Science*, "To some extent, object-oriented architecture is as much a state of mind as a state of fact." Traditional microcomputers are filled with structures called registers, which are temporary repositories of

Tale of the Orphaned Genes

Not to be outdone by the particle physicists' penchant for anthropomorphic nomenclature, molecular biologists have now coined such a term of their own: orphon. The word has been affixed to a newly discovered type of gene that is plucked from the bosom of its multigene family and set down to rest in isolation elsewhere in the genome.

In reporting their finding in *Cell*,* Geoffrey Childs, Rob Maxson, Ronald Cohn, and Larry Kedes, of the Veterans Administration Medical Center, Palo Alto, suggest that the mechanisms that generate orphons might have interesting implications for gene evolution.

"We came across orphons quite by accident," Childs told *Science*. "We were looking for late histone genes in sea urchins—the ones that are switched on shortly after hatching—and instead we found orphons of the early genes."

There are five different histone genes (H1, H4, H2B, H3, and H2A), and in the sea urchin, early histone genes are arranged as many hundreds of copies of this quintuplet in tandem repeats. The late genes are of the same five types, but their nucleotide sequences are slightly different, there are far fewer of them, and they are not clustered as multiples of the neat five-gene groups. "The new histone genes we detected are scattered all over the genome, and they are clearly derived from the early genes," says Childs, who is now at the Albert Einstein College of Medicine, New York.

The discovery of orphons poses two questions. How did they arise? And what, if anything do they do?

Research in recent years has revealed genetic material to be in a surprising state of flux: chromosomes rearrange, and stretches of DNA hop about the genome with alarming alacrity. DNA mobility is often promoted by the intervention of transposons, relatively well-defined genetic units that are able to slip in and out of chromosomes, sometimes taking passenger DNA with them. Could peripatetic transposons be responsible for translocating copies of early histone genes from the multigene family to distant parts of the genome?

This is probably not the case, conclude Childs and his colleagues. The passage of transposons leaves a very distinct trail of nucleotide sequences in the chromosomes. Although there are some hints of such sequence arrangements associated with the orphons that have been studied in detail, most of the truly telltale signs are absent.

The secret of the histone genes' translocation may lie in their family arrangement of multiple tandem repeats. The pairing of chromosomes when cells divide frequently leads to the swapping of homologous pieces of DNA between the chromosomes. The phenomenon, known as crossing over, is particularly significant when gametes are formed, as this provides a source of heritable genetic variation. Areas of the genome that contain many repeated sequences are particularly vulnerable to unequal crossing over, because the match between DNA sequences can occur at many different points. The mismatch can produce a section of DNA that is looped out, excised, and discarded.

Instead of being discarded, looped-out histone genes may, suggest Childs and his colleagues, become integrated elsewhere in the genome, and thus form orphons. Support for this view of orphon origin comes from the observation that the other well-known tandemly repeated multigene family—the ribosomal genes—also has scattered isolated relatives.

The function of orphons may be potential rather than actual. The translocation of a gene from its original functional site removes it from its family influence, with two possible consequences. One, it escapes normal control and may eventually develop its own regulatory system. "This could lead to identical or very similar genes being expressed at different times in development," guesses Childs. "Perhaps this is how the separately regulated early and late histone genes arose."

A second possible consequence is that, once outside its original genetic responsibility, an orphon's nucleotide sequence is "free" to diverge, eventually encoding information for an entirely new product.

Childs and his colleagues go further and speculate that the many dispersed (as opposed to tandemly repeated) multigene families now known might have originated as multiple orphons. "A catastrophic deletion event could eliminate the parent cluster . . . leaving behind the dispersed orphons," they write. The now truly orphaned orphons would then assume a fully independent role.

The recently recognized promiscuity of genetic material has generated an atmosphere rich in speculation about many evolutionary mechanisms. The notions proffered by the Veterans Administration group are certain to be welcomed as further possibilities for contemplation. At the very least, however, the *Cell* report indicates that "there may no longer be a clear distinction between tandem and dispersed multigene families." Orphons now occupy that middle ground.—ROGER LEWIN

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